

Amendments to the Specification:

Please replace paragraph [00020] with the following amended paragraph:

[00020] ~~Figure 5 is~~ Figures 5A and 5B are a pair of bar graphs providing data regarding HCMV CTL epitope recognition by HCMV seropositive donors.

Please replace paragraph [00021] with the following amended paragraph:

[00021] ~~Figure 6 provides~~ Figures 6A, 6B and 6C provide data regarding the recognition of three different CTL peptide analogs by HCMV seropositive donor CTL.

Please replace paragraph [00071] with the following amended paragraph:

[00071] Two separate screenings were carried out on different days for each test peptide mixture with similar results. Results from preliminary experiments (data not shown) showed that 5000 antigen presenting cells at an E:T ratio of 5 was optimal, therefore, these conditions were used to screen the PS-SCL. The results of the amidated nonapeptide PS-SCL screen are shown in ~~Figure-3~~ Figures 3A - 3I. All experimental points were obtained at the same time, and results shown represent the average of two experiments done on different days. The amidated nonapeptide PS-SCL generally gave significantly better results; mixtures at each position resulted in specific recognition and lysis. The variant peptides induced between 0 and 90% specific cytotoxicity in the

cells presenting them. Background (without peptide) was 5.0%. The highest specific cytotoxicity results for each position were approximately equivalent to the results obtained with T2 antigen presenting cells pulsed with 1.0 and 10 nM native pp65₄₉₅₋₅₀₃ epitope in a titration that was carried out simultaneously with the library screen (data not shown). In all positions the mixture having the defined amino acid that corresponds to the native peptide showed specific lysis higher than 20%. The pp65₄₉₅₋₅₀₃ epitope sensitized 50% maximal lysis of T2 cells by 3-3F4 at 0.02 nM, yet in many instances lysis exceeds 50%. There are striking levels of recognition stimulated by one or mixtures at each position. The concentration of each peptide in the loading mixture is 95.5fM, therefore the results suggest that one or more peptide(s) of high potency is responsible for the activity of the mixture.

Please replace paragraph [00075] with the following amended paragraph:

[00075] For position 6, the valine mixture is best recognized, and the second and third-ranked choices have fixed amino acids of similar structure. Position 6 likely requires a small neutral-charged amino acid for interaction with either MHC and/or TCR, independent of other substitutions. Between positions 7-9, the highest ranked mixtures are significantly better recognized than lower ranked ones. Position 7 and position 8 provide the most dramatic difference between the highest ranked mixtures, and those that follow. Significantly, mixtures which correspond to the native amino acids are substantially less recognized than the preferred mixtures. For both positions 7 and 8, there is little

correlation between the ranking of subsequent mixtures and the structure of the fixed amino acid. The recognition of the alanine and threonine mixtures at P8 are equivalent (~~Figure 3~~) (Figures 3A - 3I) which is consistent with results from the alanine-substitution study. The PS-SCL screen showed that the best mixtures had either serine or proline at position 8. Table II presents the amino acid sequences of the peptides predicted by the screen to bind to T cell clones more strongly than the native sequence.

Please replace paragraph [00076] with the following amended paragraph:

[00076] Positions 1, 3, 6 and 9 were substituted with the fixed amino acid corresponding to the top ranked mixture. In some cases, the top two amino acids were selected (as for positions 4, 5, 7 and 8) when the top two ranked mixtures were recognized almost equivalently. The 16 antigen-analogs were pulsed onto antigen presenting cells and evaluated by conducting a chromium release assay with the screening T cell clone, 3-3F4. The modified peptides were made as carboxyl-terminal amides, to be consistent with the structure of the peptides contained in the PS-SCL screening library. Two of the peptides were better recognized than the native epitope sequence by the T cell clone. These peptides (46N and 44N) were both tetra-substituted and were able to induce lysis at concentrations lower than the native epitope. Examination of the common elements of the sequence of peptides 44N and 46N, revealed a serine at position 8. This amino acid resulted in the most potent of all 20 amino acid sub-libraries tested at position 8 (~~Figure 3~~) (Figures 3A - 3I).

Interestingly, peptides 45 and 47, which share many of the substitutions of peptides 44 and 46, but which contain a proline at position 8, were less active than the native sequence. Thus, the ranking of mixtures in the initial screen conforms to the recognition properties of the individual substitution peptides tested here. A re-screen of the same T cell clone (3-3F4) by a C-terminal free acid library resulted in uniformly low recognition of all sub-libraries, even those having fixed amino acids that correspond to the native sequence (data not shown).

Please replace paragraph [00082] with the following amended paragraph:

[00082] Ten randomly selected HCMV-seropositive, HLA A*0201⁺ healthy donors were selected for evaluation to confirm that the pp65₄₉₅₋₅₀₃ CTL epitope is widely recognized by HLA A*0201 persons. The haplotypes of examined individuals are shown in Table III. A one-step *in vitro* stimulation procedure modified from Lalvani et al., J. Immunol. Meth. 210:65-77 (1997), was carried out utilizing the pp65₄₉₅₋₅₀₃ CTL epitope (SEQ ID NO:1) as the immunogen. See LaRosa et al., Blood 92(10, Suppl. 1):518a (1998). In every case, the HLA A*0201 donors provoked a specific CTL response against T2 cells, and against HCMV-infected fibroblasts. See Figure 5 5B. AD169 strain HCMV was provided by J. Zaia (City of Hope Medical Center, COH). Virus stocks of 5-10 x 10⁶ pfu/ml were prepared from the supernatant of infected MRCvhbm5 fibroblasts as previously described in Diamond et al., Blood 90:1751-1767 (1997) and used to infect dermal fibroblasts. Adherent cell lines were grown in fibroblast medium (FBM) consisting of D-MEM (Gibco, Rockville, MD) supplemented with 10%

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FBS (Hyclone, Logan, UT), 50 U/ml penicillin, 50 µg/ml streptomycin (Gibco, Rockville, MD) and 2 mM L-glutamine (Gibco, Rockville, MD). The results demonstrate that HCMV infection in HLA A*0201 positive healthy donors stimulates a specific immune response to SEQ ID NO:1 that is independent of haplotype, and likely to be universal in its expression.